* H I G H L Y C O N F I D E N T I A L *

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF NEW YORK

Civil Action File No. 14-CV-7473

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THE PEOPLE OF THE STATE OF NEW YORK, by and through ERIC T. SCHNEIDERMAN, Attorney General of the State of New York,

Plaintiff,

- against -

ACTAVIS, PLC and FOREST LABORATORIES, LLC,

Defendants.

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November 3, 2014

9:43 a.m.

Videotaped Deposition of ALAN JACOBS, pursuant to Notice, held at the offices of White & Case LLP, 1155 Avenue of the Americas, New York, New York, before Jineen Pavesi, a Registered Professional Reporter, Registered Merit Reporter, Certified Realtime Reporter and Notary Public of the State of New York.

you can answer.
A. There is lots of things we try to do; because we're titrating the medicine up from 5 milligrams to ten milligrams, for example, if the symptoms come at ten milligrams we often say stop everything, let the symptoms go away.
On a second look you may not have the same side effects and that works a lot, a large percentage of the time, but not all the time.
If we do that and even 2.5 milligrams causes side effects and we realize we can't use an oral drug like that, we might try the Excelon Patch, we would for sure if it was GI side effects, even if is the other side effects we might try because it is a different molecule and they don't always behave the same way by any means and so we would try the patch.
Interestingly enough, it is just never come to dilanthamine, the third one.
Q. Typically if a patient doesn't

respond well to donepezil, they will respond well to the Excelon Patch, and to clarify, when I say respond well, I mean in terms of side effects, not necessarily efficacy?
MR. CROWE: Objection to form, vague, calls for speculation, but you can answer.
A. Often that is the case, not always, but often.
Q. If a patient had side effects with Namenda, what would you switch them to?
MR. CROWE: Objection to form, calls for speculation and vague.
You can answer.
A. Every once in a blue moon someone put on Namenda, I will be told by their caregiver typically that they got confused, more confused, and we will stop it and see if the confusion goes away after thinking about other reasons they might have got confused, and if we end up deciding that it was the Namenda, we might

still do that, try it again once, and if it happens again we can't use it so we stop it and they can't be on Namenda.
Q. Normally would those patients be on a cholinesterase inhibitor already?
MR. CROWE: Objection to form, vague.
You can answer.
A. Typically.
Q. Is there ever a reason a patient would take both of the two cholinesterase inhibitors that you described, donepezil and rivastigmine?
MR. CROWE: Objection to form, calls for speculation, you can answer.
A. I can't imagine any situation, it would invite toxicity.
Q. But many of your patients are on both -- one of the cholinesterase inhibitors and also Namenda, correct?
A. Yes.
Q. In about how many patients is that?
MR. CROWE: Objection to form,

vague.
A. So if you take the whole universe of my patients on cholinesterase inhibitor and you restrict to the ones that have moderate to severe dementia or even are on the borderline of moderate to severe, because I will try in those situations, too, I will be adding the second drug because they are hungry for treatment and to think better and so why wouldn't you.
Q. So typically you would add Namenda to the patient's treatment regimen somewhere between the mild to moderate stage, that kind of transitional area, I know these aren't clear distinctions?
MR. CROWE: Objection to form, vague.
You can answer.
A. Typically it is moderate to severe.
For sure if I said at a meeting I think we're now into the moderate stage of this illness, I want to add a drug, but

other ways we could help that we don't have drugs yet to satisfy because it is a rich soup of neurotransmitters and what not.

Q. With regards to the timing, are these drugs typically more effective at different stages?

A. Right, so the cholinesterase inhibitor will be most effective when there is cholinergic deficiency at the same time that there is neurons around to utilize the return of acetylcholine and Namenda will be more or memantine will be more effective any time the brain cells are leaking calcium, I know we don't have a more direct way of measuring that, we assume that's the case when dementia is of moderate severity.

Q. Going back specifically to the cholinesterase inhibitors, you said that there are three that you're aware of that are actively prescribed?

A. That are on the market.

Q. Right.

Those are all distinct chemical compounds, is that correct?

A. Yes.

Q. But they are broadly the same mechanism of action, is that accurate?

MR. CROWE: Objection to form, vague, calls for speculation, but you can answer.

A. They all purport to inhibit the enzyme acetylcholinesterase.

Q. Which, again, that's distinct from what an NMDA receptor antagonist does?

A. Yes.

Q. Until now we have been talking broadly about Namenda and my understanding is that Namenda comes in basically three forms, there is the IR and the XR.

First of all, do those terms mean anything to you, IR versus XR?

A. Yes.

MR. CROWE: Objection to form.

You can answer.

Q. The IR being the

instant-release twice-a-day tablet, correct?

A. Well, the immediate release form comes in both a tablet and an elixir, two milligrams per ml, and the XR form is a once-a-day capsule filled with little caplety beads.

Q. Turning to the elixir, which sometimes I might call oral solution because that's how I think about it, do you prescribe that to any of your patients?

A. I have not prescribed it ever once to a patient.

Q. Why not?

A. The need hasn't come up.

Q. When would a patient need that particular solution?

MR. CROWE: Objection to form, vague.

You can answer.

A. One common reason has to do with -- patients with Parkinson's disease often have Alzheimer's disease and vice

versa and if you have Parkinson's disease you're very slow, you're swallowing mechanism is slow and you have poor saliva production and so it is just so much easier to have a liquid squirted into your mouth in that setting than to have to chew on a pill and get it moisturized and swallow.

There are other sorts of neurological conditions that you can imagine where chewing is hard or it may be their dentition, the person's dentition is such that it is hard and you would prefer a liquid.

But, yeah.

Q. Forgive me if you have addressed this already, but do you treat any patients with Parkinson's disease?

A. Yes.

Q. And Parkinson's and Alzheimer's disease?

A. Because I am not a movement disorder specialist, I wouldn't be seeing nearly as commonly with people just

run-of-the-mill Parkinson's, so to speak, but once they get dementia I'm often seeing them to diagnose what the nature of the dementia is, because it can be one of three things going on in that stage.

Q. Some of those patients that you treat that have Alzheimer's disease and also Parkinson's, are some of those on Namenda, one of the Namenda products?

MR. CROWE: Objection to form, you can answer.

A. To the degree they have Alzheimer's disease as the cause of their dementia, I do the same thing I do with other patients who have Alzheimer's disease, which is start with a cholinesterase inhibitor, because I am usually seeing them earlier in the phase of their dementia syndrome, and then try to get them on both drugs because that's two different types of good band-aids to help them think better.

Q. But even within those patients you have never felt the need to prescribe

the oral solution?

A. Not that I haven't felt the need, the need hasn't come up.

Q. I think you referenced that for the patients that need the oral solution, you squirt in their mouth.

What is your understanding how you administer that particular dosage form?

MR. CROWE: Objection to form, you can answer.

A. It apparently comes in a box with a syringe that you can put a top on it, interacts with a bottle and you would pull the plunger and get the amount you're going to give, which would be like 5 ccs if it is 2 milligrams per cc and you wanted to give 10 milligrams and then you would unhook it and put it at the side of the mouth and just squirt it in.

Q. Has a patient ever asked for that particular formulation in your experience?

A. Not in my experience.

MR. CROWE: Objection.

Q. Just to clarify the question, paragraph 27 of your declaration, it says "Symptomatic treatments such as memantine hydrochloride (Namenda) and cholinesterase inhibitors tend to have an additive effect to make patients think and behave more normally."

Is that correct?

A. Yes.

Q. What exactly do you mean by additive effect there?

A. It was nice to have a second drug in the symptomatic armamentarium that by virtue of addressing a different problem that brain cells have when they are afflicted with Alzheimer's disease, so to speak, seems to not just overlap such that you choose one because you're only going to get X amount of benefit regardless of which one you use, but in fact have additive benefit so that if you're cognitive scores go up X, the addition of the second drug usually makes

it go up close to 2X, and so it is additive.

Q. Do you know of any doctors that prescribe the oral solution product?

A. No, not individuals that I know by name.

I don't ask them, I haven't asked that question.

Q. Why might you keep a patient on the Namenda instant-release tablet instead of switching them to the XR capsule?

MR. CROWE: Objection to form, lack of foundation, vague, and calls for speculation.

But you can answer.

A. Once the XR came out, it became pretty obvious that that would be preferable because of it's once-a-day dosing regimen.

So if I haven't seen someone yet, I wouldn't be calling them up and say come in, I want to give you XR, I would typically wait until they come in for followup and see they are on the IR drug

version of the Namenda IR product, the tablet specifically, would be entering the market, is that correct?

A. What I said was I assumed it would be because, just like I assumed any medicine eventually loses its patent and generics come onboard and that generic drugs exist and therefore any given drugs will eventually go generic.

I didn't have specific knowledge of when Namenda would prior to any of this.

Q. Do you normally receive marketing materials or detailing from branded drug manufacturers?

MR. CROWE: Objection to form.

You can answer.

A. No; I get things in the mail and I usually just throw them right away because I am not going to bother with anything like that, that's just sort of not medical information.

Q. You don't get like the pens or the pads?

A. I still have a box of Aricept pens in my office that was given to me in 1996 with so many pens that I am never going to run out.

So I never needed anymore pens.

Q. What about from generic drug companies, do you get any marketing information or pens from those firms?

MR. CROWE: Objection, vague.

You can answer.

A. I don't remember ever getting -- I don't know anything about generic companies honestly, never heard of one.

Q. You can't name a single generic company?

A. Not at all.

Q. What about patients, are patients typically aware of generic drugs when they come into your office?

MR. CROWE: Objection to form, vague, calls for speculation, but you can answer.

Q. In your experience.

A. We have discussions all the time, it happens a lot in neuroendocrinology because those patients are young and they are not wealthy and they care a lot about cost issues and they may say something like I want the generic and I might say, you know what, we should do the brand first for a while because phamacokinetics are well-described and standardized and then, assuming we can get the dose response that we want and we like the efficacy and you don't have side effects, then you can switch to the generic because then we'll know if there is a difference.

And if there is a difference, you'll have data to say to your insurance company, you ought to pay for this brand because it works better.

So that happens a lot in that setting, I can't remember -- I think I also remember when Aricept went generic, everyone was happy, my patients were happy, because now they were just getting

the donepezil and we learned quickly there was no difference, it was less expensive and worked the same.

Q. Specifically with the neuroendocrinology context, was it the patient that initiated the discussion about the generics or did you inform them that there was a generic available and that you would try this treatment strategy?

MR. CROWE: Objection, form, vague and calls for speculation.

You can answer.

A. I mean, over time in the 20 years I have been practicing medicine, really the ten years I have been in private practice, where people give me money to see me and I have to feel like I owe them as much benefit as I can give them, I've become more and more aware to the point where I often initiate that and say, you know, I am going to give you this and I have a discussion about why I might want to -- I say would you rather have